Hurst LC, Badalemente MA, et al. Injectable Collagenase Clostridium Histolyticum for Dupuytren's Contracture. N Engl J Med 2009;361:968-79.

Design: Randomized Phase III clinical trial

Population/sample size/setting:

- 308 patients (245 men, 63 women, mean age 63) with Dupuytren's contracture of 20° or more participating in a Phase III trial of injectable collagenase at several academic centers in the US
- Eligibility criteria were good general health, age over 18, with MP joint contractures between 20° and 100°, or PIP contractures between 20°and 80°
- Exclusion criteria were pregnancy, breast feeding, bleeding disorder, recent stroke, treatment of the joint within 90 days before start of study, use of tetracycline within 7 days before start of study, chronic muscle or nerve disorder, and allergy to collagenase

Main outcome measures:

- Randomized to injection with 0.58 mg. collagenase clostridium histolyticum (n=204) or placebo (n=104), with stratification for severity of contracture (<=50° vs. >50°) and joint primarily affected (MP vs. PIP
- Injections were done directly into affected cord with joint manipulation up to 3 times the day after the procedure to rupture the cords; patients received a splint for night use up to 4 months, but no hand therapy was done
- A maximum of 3 injections could be done, with 30 days of follow-up between each injection
- Follow-up assessments were done 30 days after last injection and 30 days after first injection
- Primary end point was "success" defined as present when primary joint contracture was reduced to 0°to 5° 30 days after last injection
- Numerous secondary end points were measured; these included grip strength, time to reduction of contracture, change in range of motion, and clinical improvement (reduction of contracture 50% or more from baseline)
- "Success" was observed in 64% of collagenase patients and in 6.8% of placebo patients 30 days after last injection
- Reduction of contracture to less than 5° was observed within 30 days of first injection in 39.9% of collagenase and 1% of placebo injection patients
- Mean change in contracture from baseline to 30 days after last injection was from 50.2° to 12.2° in the collagenase group, and from 49.1° to 45.7° in the placebo group
- Adverse events occurred in almost all (96.6%) of collagen patients and in 21.2% of placebo patients; most common were contusion, injection-site pain and/or hemorrhage, tenderness, pruritus, swelling; 3 serious adverse events occurred in collagenase group: 1 case of CRPS and 2 tendon ruptures requiring surgical intervention

- No allergic reactions were seen, but neutralizing antibody against type I collagen clostridium histolyticum did develop in most patients who received this injection by 90° after the final injection

Authors' conclusions:

- Injectable collagen clostridium histolyticum is safe and effective in patients with advanced Dupuytren's disease
- The 30 day outcomes indicate that collagen clostridium histolyticum may provide an alternative to surgery
- No recurrence of contracture was seen in the 30 day follow-up period; this may be too short to assess recurrence, and no claims to that effect are made

Comments:

- Treatment effect size was large in both PIP and MP joints
- A few points are not clearly delineated: there were four subgroups randomized to placebo or collagenase (MP and PIP, <50° and >50°), but the numbers randomized in each of these groups is not specified
- Adverse effects appear to be very common, even if few are serious
- Adverse effect risk would need to be discussed and clearly explained to patients considered for the injection
- Further follow-up data will be required to determine recurrence rate

Assessment: High-quality for an evidence statement that collagen clostridium histolyticum injections may significantly reduce contracture in patients with Dupuytren's disease